

# Inherited anaemias in the Greek community of Cape Town

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**SUMMARY** Cape Town has a Greek community of about 5000, of whom approximately 75% originate from the island of Lesbos. In a survey of inherited haematological conditions in this population, 250 unrelated volunteers were investigated.

The prevalence of heterozygous  $\beta$ -thalassaemia was found to be 6.4%, with a gene frequency of 0.033. G6PD deficiency was detected in 10 males and it can be estimated that the prevalence in the male members of this population is 6.7%, with a gene frequency of 0.067. Hereditary spherocytosis was found in three respondents and this represents a prevalence of 1.2%, with a gene frequency of 0.006. One subject was heterozygous for the sickle cell trait (HbS) and another volunteer had haemoglobin Lepore, which had already been diagnosed in Greece.

Our findings with respect to  $\beta$ -thalassaemia and G6PD deficiency are similar to those reported from regions in Greece where malaria is not highly endemic.

Every well-defined population has a particular pattern of genetic disorders. Inherited anaemias, notably glucose-6-phosphate dehydrogenase deficiency (G6PD),  $\beta$ -thalassaemia, and spherocytosis occur with significant frequency in people of Greek stock in South Africa.

Programmes for management, control, and prevention of inherited conditions are dependent upon basic information concerning the prevalence and clinical consequences of the disorders in question. For these reasons we have undertaken a survey of familial haematological disorders in the Greek community of Cape Town. Our findings are presented and discussed in this paper.

## Demography

The first Greeks to visit South Africa were seamen, who arrived in the middle of the last century. Following the discovery of diamonds and gold, there was a general influx of immigrants from many countries, and by 1900 Cape Town had a Greek population of approximately 1000. At this time a Greek orthodox priest from Crete was sent to Cape Town to found a Greek community, and in the following decade additional communities were

established in Johannesburg and Pretoria (Nickolaides, 1923).

In 1915, 1500 Greeks lived in Cape Town but many left to fight in the first world war and by 1925 only 250 remained. The population subsequently slowly increased to reach 1000 by 1961. At this time immigration offices were opened to attract immigrants to South Africa, and Cape Town, with a population of just over one million people, now has a Greek population of about 5000. Between 70% and 80% of the immigrants originated from the island of Lesbos, while the remainder came from Cyprus, Lemnos, Cephalonia, Athens, and the Peloponnese (S. Papassavas, 1977, personal communication).

The reason for the high proportion of immigrants with antecedents in Lesbos in Cape Town is the fact that one of the first Greek immigrants was from this island. He brought out his brothers, who in turn attracted their cousins. This practice continued, with immigrants encouraging their family and friends to emigrate to Cape Town. The immigration of people from other parts of Greece was influenced by similar considerations, but took place on a smaller scale.

At present, the Greek population of South Africa numbers approximately 65 000 and 50 000 Greeks live in Johannesburg and on the Witwatersrand. Durban and Port Elizabeth have communities of

about 2000 and small numbers of Greeks live in the majority of towns in South Africa.

## Methods

Demographic information concerning the Greek population living in Cape Town and other parts of South Africa was obtained from ecclesiastical and secular leaders of the Greek community and from the government departments of information and health.

A letter was sent to all Greeks in Cape Town explaining the aims and purpose of the study and prospective subjects were invited to volunteer for blood sampling. Members of the Greek community were addressed at a cinema club where they met regularly. At subsequent film evenings a slide concerning the study was shown as a reminder. A further source of respondents was the in-patients of Greek stock at Groote Schuur Hospital who had been admitted for non-haematological disorders. Ascertainment continued until 250 unrelated respondents, representing 5% of the community, had been studied. These comprised 150 males and 100 females.

A brief clinical history was obtained from each volunteer, with emphasis on anaemia, jaundice, gallstones, malaria, and drug reactions. Respondents were examined if an inherited haematological disorder was suspected, and in these circumstances special attention was paid to the presence or absence of hepatosplenomegaly.

A 20 ml venous blood specimen was obtained from each of the respondents for haematological and biochemical investigations. The following standard laboratory procedures were undertaken.

- (1) Peripheral blood smears: red cell morphology.
- (2) Supravital stained preparations: (a) reticulocytes, (b) haemoglobin H inclusion bodies.
- (3) Red cell parameters: (a) haemoglobin level, (b) packed cell volume, (c) red cell count, (d) mean corpuscular haemoglobin concentration, (e) mean corpuscular volume, (f) mean corpuscular haemoglobin.
- (4) Osmotic fragility.
- (5) Electrophoresis: (a) abnormal haemoglobins (Lehmann and Ager, 1960), (b) quantification of haemoglobin A<sub>2</sub> (Black *et al.*, 1966).
- (6) Quantification of haemoglobin F (Singer *et al.*, 1951).
- (7) Brilliant cresyl blue dye test (Motulsky and Campbell-Kraut, 1961).
- (8) Methaemoglobin reduction test for G6PD deficiency (Brewer *et al.*, 1962).
- (9) Solubility test for haemoglobin S (Itano, 1953).
- (10) Autohaemolysis studies if spherocytosis was suspected (Dacie and Lewis, 1975).

The requirements for recognising  $\beta$ -thalassaemia trait were: abnormality in 2 of 3 haematological criteria, (a) red cell morphology, (b) increased osmotic resistance, (c) decreased mean cell haemoglobin; and abnormality in one of the biochemical criteria, (a) increase in haemoglobin A<sub>2</sub> above 3%, (b) increase in haemoglobin F above 2%. For the diagnosis of  $\alpha$ -thalassaemia trait, a search for red cell inclusion bodies of haemoglobin H type was added to the haematological criteria, of which 3 of 4 had to be abnormal and, as biochemical criterion, the presence of a fast-moving haemoglobin was substituted for abnormality of haemoglobin A<sub>2</sub> or haemoglobin F.

The method of Black *et al.* (1966) for estimating haemoglobin A<sub>2</sub> was used for economy, but a random 10% of all specimens, as well as abnormal specimens, were retested by elution from cellulose-acetate. Discrepancies did not occur.

For the diagnosis of haemoglobin S, both paper and agar electrophoresis were applied, and decreased solubility was shown by Itano's test (Itano, 1953). For G6PD activity, the test of Motulsky and Campbell-Kraut (1961) was used; in the case of females with minimally prolonged test times, methaemoglobin reduction (Brewer *et al.*, 1962) was used for confirmation.

Hereditary spherocytosis was recognised by a combination of increased osmotic fragility, particularly after incubation at 37° for 24 hours; increased autohaemolysis after similar incubation, which was corrected or much decreased by the addition of glucose; and the presence of a proportion of microspherocytes in the peripheral blood. From the random nature of the survey it proved difficult to arrange family investigations which may have given confirmation in the doubtful instances.

## Results

The following haematological disorders were identified among the 250 respondents from the Greek population of Cape Town.

### (a) THALASSAEMIA

Sixteen people heterozygous for  $\beta$ -thalassaemia were diagnosed on haematological and biochemical grounds. The overall prevalence of heterozygous  $\beta$ -thalassaemia in the Greek community was 6.4%, with a gene frequency of 0.032. Not included in the 250 random subjects, but previously encountered, were two locally born subjects of Greek origin with homozygous  $\beta$ -thalassaemia (thalassaemia major). When a distinction is made (Kattamis *et al.*, 1978) between heterozygous  $\beta$ -thalassaemia (with increased haemoglobin A<sub>2</sub> and haemoglobin F less

than 5%) and heterozygous  $\delta\beta$ -thalassaemia (with normal haemoglobin A<sub>2</sub> and haemoglobin F increased above 5%), the latter condition was not recognised in the random sample. However,  $\delta\beta$ -thalassaemia trait was previously recognised locally in two instances. Found during the survey was a subject with normal haemoglobin A<sub>2</sub> and slightly raised haemoglobin F with haematological stigmata in keeping with heterozygous  $\beta$ -thalassaemia. This may represent the type of thalassaemia trait with no, or only slight, biochemical abnormality, but which may nevertheless interact with the classical  $\beta$ -thalassaemia trait to produce the full picture of homozygous  $\beta$ -thalassaemia (Malamos *et al.*, 1962; Kattamis *et al.*, 1978). The ratio of  $\beta$ -thalassaemia trait to  $\delta\beta$ -thalassaemia trait in Greece, calculated from data of Malamos *et al.* (1962) and Kattamis *et al.* (1978), is approximately of the order of 10:1. One might, therefore, have expected to find a  $\delta\beta$ -heterozygote in the present survey.

$\alpha$ -thalassaemia was not recognised in this study, but the gene is known to be present among local Greeks from previous cord blood surveys (M. C. Botha, 1978, unpublished data).

#### (b) G6PD DEFICIENCY

Thirteen subjects were found to have G6PD deficiency. Of these, 10 were male and 3 female. The prevalence of G6PD deficiency in the males was 6.7%, with a gene frequency of 0.067. These figures have been calculated only for the males, as the diagnosis can be missed in a proportion of heterozygous females.

#### (c) HEREDITARY SPHEROCYTOSIS

Of the 250 subjects, 3 were found to have hereditary spherocytosis and the prevalence of this condition was 1.2%, with a gene frequency of 0.006. Four other people in the survey had laboratory findings which were highly suggestive of hereditary spherocytosis, but the diagnosis could not be established with absolute certainty. On this basis, the prevalence could be as high as 2.5%, with a corresponding gene frequency of 0.0125.

#### (d) HAEMOGLOBINOPATHIES

One subject had the sickle cell trait (heterozygous for haemoglobin S). The prevalence was 0.4%, with a gene frequency of 0.002.

A recent immigrant volunteered for the survey with the knowledge that he had haemoglobin Lepore, initially diagnosed in Greece.

### Discussion

The frequency of the gene for  $\beta$ -thalassaemia was within the range found in Greece. In a random

population study an incidence of 7.44% was reported (Malamos *et al.*, 1962), and in a regional study, based on malarial endemicity, the frequency ranged from 6.1 to 19.7% with a mean of 14.25% (Stamatoyannopoulos and Fessas, 1964). The frequency of G6PD deficiency among Greeks in Cape Town was similar to that found in areas of Greece where malaria was not highly endemic, the prevalence being reported as 3.3% in malaria-free areas, 4.5% in moderately endemic regions, and 19.8% in several endemic regions. Information specific to Lesbos was not found, but it is noteworthy that the prevalence of G6PD deficiency on islands such as Corfu and Serifos is low or the condition is absent (Stamatoyannopoulos and Fessas, 1964).

The considerable discrepancies in the frequency of these genes in various parts of Greece is probably a reflection of biological advantage in terms of protection against malaria, which was, until recently, endemic in the Greek islands (Motulsky, 1960). From this, two considerations arise. If malaria represents the environmental pressure which was required to maintain this balanced polymorphism, the genes for thalassaemia and G6PD deficiency should gradually be lost from the local Greek community; and, in view of the demographic structure of the Greek population in South Africa, the findings in Cape Town cannot necessarily be extrapolated to other centres in South Africa, where the Greek communities have different origins. Nevertheless, it is reasonable to assume that the inherited anaemias which we have encountered will be present in significant prevalence in all Greek groups in South Africa.

From the practical point of view, the form of G6PD deficiency in the Greek population is usually a mild disease which causes little morbidity, and haemolysis on exposure to certain drugs is the major complication. However, two subjects in our series had previously experienced acute haemolytic crises which necessitated urgent hospital admission, and on this basis the condition certainly has clinical significance.

Laboratory diagnosis is comparatively easy and population screening would be worthwhile, as identification of affected people could form the basis for prevention by avoidance of known precipitating factors. Subjects identified during our survey were informed of these hazards and given a list of medicines which were contraindicated. This information was also passed on to their general practitioners.

Homozygous  $\beta$ -thalassaemia is a serious disease which causes considerable disability and compromises the life span. The heterozygous carrier of the abnormal gene frequently is virtually asymptomatic,

but recognition of 'at risk' couples by population screening merits consideration now that antenatal diagnosis of the condition is feasible (Hobbins and Mahoney, 1974; Fairweather *et al.*, 1978).

Spherocytosis does not always cause clinical problems and may only be detected in laboratory investigation of relatives of patients with overt symptoms. However, there is a risk of episodes of anaemia and an increased incidence of cholelithiasis as a result of chronic haemolysis. The prevalence of spherocytosis in the Greek community of Cape Town is much higher than the figure of 1/10 000 which is quoted for Europe. There are no comparable data for the Mediterranean region, but it is reasonable to speculate that the founder effect has been operative.

It is generally accepted that unexplained anaemia in a subject of Greek stock in South Africa should arouse suspicion of a familial disorder of this type. Confirmation of the relatively high prevalence of these hereditary conditions by this survey provides a scientific basis for this clinical attitude.

We are grateful to Mr J. Rees, Mrs I. Udrzal, and Mrs C. Zarvos of the Cape Provincial Blood Grouping Laboratory for the laboratory studies. We thank Mr Papassavas and Mrs Saridakis, respectively teacher and secretary to the Greek community, for their co-operation during the survey. For the preparation of the manuscript we are indebted to Mrs B. Breytenbach.

We acknowledge with thanks grants from the University of Cape Town Staff Research Fund and the South African Medical Research Council.

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